

Applicant : Stephen Thom et al.  
 Serial No. : 10/069,215  
 Filed : February 22, 2002  
 Page : 2 of 11

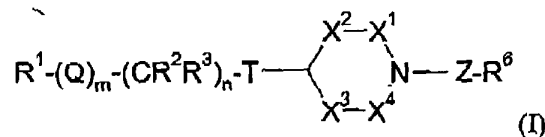
Attorney's Docket No.: 06275-244US1 / A 2214-1P US

### Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

### Listing of Claims:

1. (Presently amended) ~~The present invention provides a~~ Δ compound of formula (I), or a pharmaceutically acceptable salt thereof, or solvate thereof, or a solvate of a salt thereof:



wherein

Z is  $CR^4R^5$ ,  $C(O)$  or  $CR^4R^5-Z^+$ , wherein  $R^4$  and  $R^5$  are  $CH_2$ ;

$Z^+$  is  $C_{1-4}$  alkylene,  $C_{2-4}$  alkenylene or  $C(O)NH$ ;

$R^+$  represents a  $C_1$ - $C_{12}$  alkyl group optionally substituted by one or more substituents independently selected from cyano, hydroxyl,  $C_1$ - $C_6$  alkoxy,  $C_1$ - $C_6$  alkylthio,  $C_2-7$  cycloalkyl,  $C_1$ - $C_6$  alkoxy carbonyl and phenyl (itself optionally substituted by one or more of halogen, nitro, cyano,  $C_1$ - $C_6$  alkyl,  $C_1$ - $C_6$  haloalkyl, phenyl( $C_1$ - $C_6$  alkyl),  $C_1$ - $C_6$  alkoxy,  $C_1$ - $C_6$  haloalkoxy,  $S(O)_2$ ( $C_1$ - $C_6$  alkyl),  $C(O)NH_2$ , carboxy or  $C_1$ - $C_6$  alkoxy carbonyl); or

$R^+$  represents  $C_2$ - $C_6$  alkenyl optionally substituted by phenyl (itself optionally substituted by one or more of halogen, nitro, cyano,  $C_1$ - $C_6$  alkyl,  $C_1$ - $C_6$  haloalkyl, phenyl( $C_1$ - $C_6$  alkyl),  $C_1$ - $C_6$  alkoxy,  $C_1$ - $C_6$  haloalkoxy,  $S(O)_2$ ( $C_1$ - $C_6$  alkyl),  $C(O)NH_2$ , carboxy or  $C_1$ - $C_6$  alkoxy carbonyl); or

$R^1$  represents a 3- to 14-membered saturated or unsaturated ring system which optionally comprises up to two ring carbon atoms that form carbonyl groups and which optionally further comprises up to 4 ring heteroatoms independently selected from nitrogen, oxygen and sulphur, wherein the ring system is optionally substituted by one or more substituents independently selected from: halogen, cyano, nitro, oxo, hydroxyl,  $C_1$ - $C_8$  alkyl,  $C_1$ - $C_6$  hydroxyalkyl,  $C_1$ - $C_6$  haloalkyl,  $C_1$ - $C_6$  alkoxy( $C_1$ - $C_6$  alkyl),  $C_3$ - $C_7$  cycloalkyl( $C_1$ - $C_6$  alkyl),  $C_1$ - $C_6$  alkylthio( $C_1$ - $C_6$  alkyl),

Applicant : Stephen Thom et al.  
 Serial No. : 10/069,215  
 Filed : February 22, 2002  
 Page : 3 of 11

Attorney's Docket No.: 06275-244US1 / A 2214-1P US

C<sub>1</sub>-C<sub>6</sub> alkylcarbonyloxy(C<sub>1</sub>-C<sub>6</sub> alkyl), C<sub>1</sub>-C<sub>6</sub> alkylS(O)<sub>2</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), aryl(C<sub>1</sub>-C<sub>6</sub> alkyl), heterocyclyl(C<sub>1</sub>-C<sub>6</sub> alkyl), arylS(O)<sub>2</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), heterocyclylS(O)<sub>2</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)S(O)<sub>2</sub>, heterocyclyl(C<sub>1</sub>-C<sub>6</sub> alkyl)S(O)<sub>2</sub>, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, carboxy-substituted C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>1</sub>-C<sub>6</sub> haloalkoxy, C<sub>1</sub>-C<sub>6</sub> hydroxyalkoxy, C<sub>1</sub>-C<sub>6</sub> alkylcarboxy-substituted C<sub>1</sub>-C<sub>6</sub> alkoxy, aryloxy, heterocyclyloxy, C<sub>1</sub>-C<sub>6</sub> alkylthio, C<sub>3</sub>-C<sub>7</sub> cycloalkyl(C<sub>1</sub>-C<sub>6</sub> alkylthio), C<sub>3</sub>-C<sub>6</sub> alkynylthio, C<sub>1</sub>-C<sub>6</sub> alkylcarbonylamino, C<sub>1</sub>-C<sub>6</sub> haloalkylcarbonylamino, SO<sub>3</sub>H, -NR<sup>7</sup>R<sup>8</sup>, -C(O)NR<sup>23</sup>R<sup>24</sup>, S(O)<sub>2</sub>NR<sup>18</sup>R<sup>19</sup>, S(O)<sub>2</sub>R<sup>20</sup>, R<sup>25</sup>C(O), carboxyl, C<sub>1</sub>-C<sub>6</sub> alkoxy-carbonyl, aryl and heterocyclyl; wherein the foregoing aryl and heterocyclyl moieties are optionally substituted by one or more of halogen, oxo, hydroxy, nitro, cyano, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> haloalkyl, phenyl(C<sub>1</sub>-C<sub>6</sub> alkyl), C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>1</sub>-C<sub>6</sub> haloalkoxy, S(O)<sub>2</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), C(O)NH<sub>2</sub>, carboxy or C<sub>1</sub>-C<sub>6</sub> alkoxy-carbonyl;

m is 0 or 1;

Q represents an oxygen or sulphur atom or a group NR<sup>9</sup>, C(O), C(O)NR<sup>9</sup>, NR<sup>9</sup>C(O) or CH=CH; n is 0, 1, 2, 3, 4, 5 or 6 provided that when n is 0, then m is 0;

each R<sup>2</sup> and R<sup>3</sup> independently represents a hydrogen atom or a C<sub>1</sub>-C<sub>4</sub> alkyl group, or (CR<sup>2</sup>R<sup>3</sup>)<sub>n</sub> represents C<sub>3</sub>-C<sub>7</sub> cycloalkyl optionally substituted by C<sub>1</sub>-C<sub>4</sub> alkyl;

T represents a group NR<sup>10</sup>, C(O)NR<sup>10</sup>, NR<sup>11</sup>C(O)NR<sup>10</sup> or C(O)NR<sup>10</sup>NR<sup>11</sup>, wherein R<sup>10</sup> is H;

X<sup>1</sup>, X<sup>2</sup>, X<sup>3</sup> and X<sup>4</sup> are, independently, CH<sub>2</sub>, CHR<sup>12</sup> (wherein each R<sup>12</sup> is, independently, C<sub>1</sub>-C<sub>4</sub> alkyl or C<sub>3</sub>-C<sub>7</sub> cycloalkyl(C<sub>1</sub>-C<sub>4</sub> alkyl)) or C=O; or, when they are CHR<sup>12</sup>, the R<sup>12</sup> groups of X<sup>1</sup> and X<sup>3</sup> or X<sup>4</sup>, or X<sup>2</sup> and X<sup>3</sup> or X<sup>3</sup> and X<sup>4</sup> join to form a two or three atom chain which is CH<sub>2</sub>CH<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>, CH<sub>2</sub>OCH<sub>2</sub> or CH<sub>2</sub>SCH<sub>2</sub>; provided always that at least two of X<sup>1</sup>, X<sup>2</sup>, X<sup>3</sup> and X<sup>4</sup> are CH<sub>2</sub>;

R<sup>4</sup> and R<sup>5</sup> each independently represent a hydrogen atom or a C<sub>1</sub>-C<sub>4</sub> alkyl group;

R<sup>6</sup> is aryl or heterocyclylphenyl, both optionally substituted by one or more of: halogen, cyano, nitro, oxo, hydroxyl, C<sub>1</sub>-C<sub>8</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> hydroxyalkyl, C<sub>1</sub>-C<sub>6</sub> haloalkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy(C<sub>1</sub>-C<sub>6</sub> alkyl), C<sub>3</sub>-C<sub>7</sub> cycloalkyl(C<sub>1</sub>-C<sub>6</sub> alkyl), C<sub>1</sub>-C<sub>6</sub> alkylthio(C<sub>1</sub>-C<sub>6</sub> alkyl), C<sub>1</sub>-C<sub>6</sub> alkylcarbonyloxy(C<sub>1</sub>-C<sub>6</sub> alkyl), C<sub>1</sub>-C<sub>6</sub> alkylS(O)<sub>2</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), aryl(C<sub>1</sub>-C<sub>6</sub> alkyl), heterocyclyl(C<sub>1</sub>-C<sub>6</sub> alkyl), arylS(O)<sub>2</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), heterocyclylS(O)<sub>2</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)S(O)<sub>2</sub>, heterocyclyl(C<sub>1</sub>-C<sub>6</sub>

Applicant : Stephen Thom et al.  
Serial No. : 10/069,215  
Filed : February 22, 2002  
Page : 4 of 11

Attorney's Docket No.: 06275-244US1 / A 2214-1P US

alkyl)S(O)<sub>2</sub>, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, carboxy-substituted C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>1</sub>-C<sub>6</sub> haloalkoxy, C<sub>1</sub>-C<sub>6</sub> hydroxyalkoxy, C<sub>1</sub>-C<sub>6</sub> alkylcarboxy-substituted C<sub>1</sub>-C<sub>6</sub> alkoxy, aryloxy, heterocycloxy, C<sub>1</sub>-C<sub>6</sub> alkylthio, C<sub>3</sub>-C<sub>7</sub> cycloalkyl(C<sub>1</sub>-C<sub>6</sub> alkylthio), C<sub>3</sub>-C<sub>6</sub> alkynylthio, C<sub>1</sub>-C<sub>6</sub> alkylcarbonylamino, C<sub>1</sub>-C<sub>6</sub> haloalkylcarbonylamino, SO<sub>3</sub>H, -NR<sup>16</sup>R<sup>17</sup>, -C(O)NR<sup>21</sup>R<sup>22</sup>, S(O)<sub>2</sub>NR<sup>13</sup>R<sup>14</sup>, S(O)<sub>2</sub>R<sup>15</sup>, R<sup>26</sup>C(O), carboxyl, C<sub>1</sub>-C<sub>6</sub> alkoxy-carbonyl, aryl and heterocyclyl; wherein the foregoing aryl and heterocyclyl moieties are optionally substituted by one or more of halogen, nitro, cyano, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> haloalkyl, phenyl(C<sub>1</sub>-C<sub>6</sub> alkyl), C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>1</sub>-C<sub>6</sub> haloalkoxy, S(O)<sub>2</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), C(O)NH<sub>2</sub>, carboxy or C<sub>1</sub>-C<sub>6</sub> alkoxy-carbonyl; R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup>, R<sup>10</sup>, R<sup>11</sup>, R<sup>13</sup>, R<sup>14</sup>, R<sup>16</sup>, R<sup>17</sup>, R<sup>18</sup>, R<sup>19</sup>, R<sup>21</sup>, R<sup>22</sup>, R<sup>23</sup> and R<sup>24</sup> are, independently hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> haloalkyl, C<sub>1</sub>-C<sub>6</sub> hydroxyalkyl, C<sub>3</sub>-C<sub>7</sub> cycloalkyl, C<sub>3</sub>-C<sub>7</sub> cycloalkyl(C<sub>1</sub>-C<sub>4</sub> alkyl) or phenyl(C<sub>1</sub>-C<sub>6</sub> alkyl); and, R<sup>15</sup> and R<sup>20</sup> are, independently, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> hydroxyalkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, C<sub>3</sub>-C<sub>7</sub> cycloalkyl(C<sub>1</sub>-C<sub>4</sub> alkyl) or C<sub>1</sub>-C<sub>6</sub> alkyl optionally substituted by phenyl; R<sup>25</sup> and R<sup>26</sup> are, independently, C<sub>1</sub>-C<sub>6</sub> alkyl or phenyl (optionally substituted by one or more of halogen, nitro, cyano, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> haloalkyl, phenyl(C<sub>1</sub>-C<sub>6</sub> alkyl), C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>1</sub>-C<sub>6</sub> haloalkoxy, S(O)<sub>2</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), C(O)NH<sub>2</sub>, carboxy or C<sub>1</sub>-C<sub>6</sub> alkoxy-carbonyl); or a pharmaceutically acceptable salt thereof, or solvate thereof, or a solvate of a salt thereof; provided that when T is C(O)NR<sup>10</sup> and R<sup>1</sup> is optionally substituted phenyl then n is not 0.

2-4. (Cancelled)

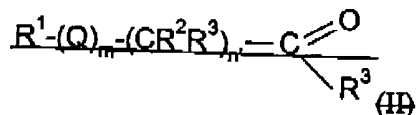
5. (Original) A compound as defined in any one of Examples 1 to 416.

6. (Presently amended) A process for the preparation of a compound of formula (I) as defined in claim 1 which comprises:

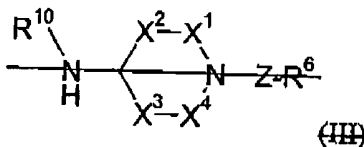
(a) ~~when n is at least 1, the CR<sup>2</sup>R<sup>3</sup> group attached directly to T is CHR<sup>2</sup> and T is NR<sup>10</sup>, reacting a compound of general formula~~

Applicant : Stephen Thom et al.  
 Serial No. : 10/069,215  
 Filed : February 22, 2002  
 Page : 5 of 11

Attorney's Docket No.: 06275-244US1 / A 2214-1P US

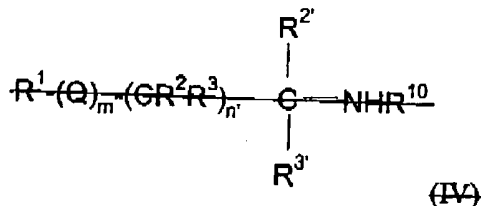


wherein  $n'$  is 0 or an integer from 1 to 3 and  $R^1, R^2, R^3, m$  and  $Q$  are as defined in formula (I), with a compound of general formula

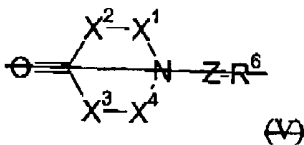


or a salt thereof, wherein  $X^1, X^2, X^3, X^4, Z, R^6$  and  $R^{10}$  are as defined in formula (I), in the presence of a reducing agent; or

(b) — when  $n$  is at least 1, the  $CR^2R^3$  group attached directly to T is  $C(C_1-C_4 \text{ alkyl})_2$  and T is  $NR^{10}$ , reacting a compound of general formula



wherein  $n'$  is 0 or an integer from 1 to 3,  $R^2$  and  $R^3$  each independently represent a  $C_1-C_4$  alkyl group, and  $R^1, R^2, R^3, R^{10}, m$  and  $Q$  are as defined in formula (I), with a compound of general formula

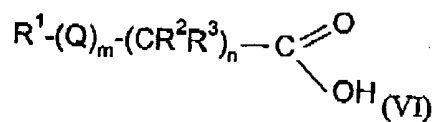


wherein  $X^1, X^2, X^3, X^4, Z$  and  $R^6$  are as defined in formula (I), in the presence of a reducing agent; or

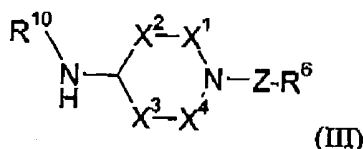
Applicant : Stephen Thom et al.  
 Serial No. : 10/069,215  
 Filed : February 22, 2002  
 Page : 6 of 11

Attorney's Docket No.: 06275-244US1 / A 2214-1P US

(ea) when T is C(O)NR<sup>10</sup>, reacting a compound of general formula

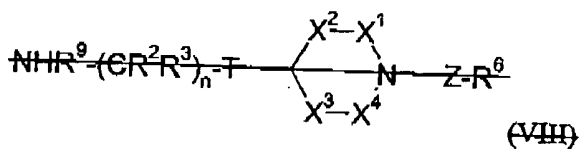


wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, Q, m and n are as defined in formula (I), with a compound of formula (III)



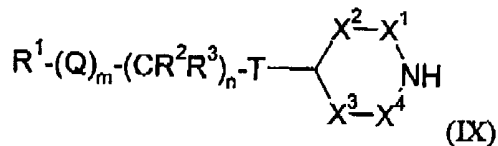
wherein X<sup>1</sup>, X<sup>2</sup>, X<sup>3</sup>, X<sup>4</sup>, Z, R<sup>6</sup> and R<sup>10</sup> are as defined in formula (I), or a salt thereof as defined in (a) above; or

~~(d) when m is 1 and Q is NR<sup>9</sup>, reacting a compound of general formula (VII), R<sup>1</sup>-L<sup>+</sup>, wherein L<sup>+</sup> represents a leaving group (e.g. a halogen atom) and R<sup>1</sup> is as defined in formula (I), with a compound of general formula~~



~~or a salt thereof, wherein n, T, X<sup>1</sup>, X<sup>2</sup>, X<sup>3</sup>, X<sup>4</sup>, Z, R<sup>2</sup>, R<sup>3</sup>, R<sup>6</sup> and R<sup>9</sup> are as defined in formula (I); or~~

(eb) when at least one of R<sup>4</sup> and R<sup>5</sup> represents a hydrogen atom, reacting a compound of general formula

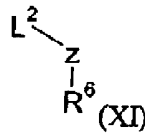


Applicant : Stephen Thorn et al.  
 Serial No. : 10/069,215  
 Filed : February 22, 2002  
 Page : 7 of 11

Attorney's Docket No.: 06275-244US1 / A 2214-1P US

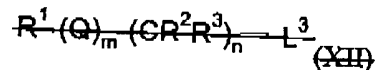
or a salt thereof, wherein  $R^1$ ,  $R^2$ ,  $R^3$ ,  $Q$ ,  $m$ ,  $n$ ,  $X^1$ ,  $X^2$ ,  $X^3$ ,  $X^4$  and  $T$  are as defined in formula (I), with a compound of general formula (X),  $R^6 - C(O) - R^{20}$ , wherein  $R^{20}$  represents a hydrogen atom or a  $C_1$ - $C_4$  alkyl group and  $R^6$  is as defined in formula (I), in the presence of a reducing agent; or

(fc) reacting a compound of formula (IX) as defined in (e)(b) above, with a compound of general formula



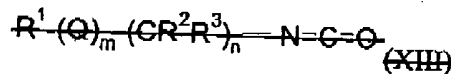
wherein  $L^2$  represents a leaving group (e.g. a halogen atom) and  $Z$  and  $R^6$  are as defined in formula (I); or

(g) when  $T$  is  $NR^{10}$ , reacting a compound of general formula



wherein  $L^3$  represents a leaving group (e.g. a halogen atom) and  $R^1$ ,  $R^2$ ,  $R^3$ ,  $m$ ,  $n$  and  $Q$  are as defined in formula (I), with a compound of formula (III) or a salt thereof as defined in (a) above; or

(h) when  $T$  is  $NHC(O)NR^{10}$ , reacting a compound of general formula

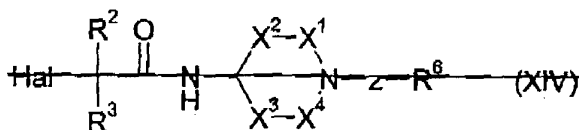


wherein  $R^1$ ,  $R^2$ ,  $R^3$ ,  $Q$ ,  $m$  and  $n$  are as defined in formula (I), with a compound of formula (III) or a salt thereof as defined in (a) above; or

Applicant : Stephen Thom et al.  
 Serial No. : 10/069,215  
 Filed : February 22, 2002  
 Page : 8 of 11

Attorney's Docket No.: 06275-244US1 / A 2214-1P US

(i) ~~when T is C(O)NH, Z is CH<sub>2</sub>, n is 1, R<sup>2</sup> and R<sup>3</sup> are hydrogen or C<sub>1</sub>-C<sub>4</sub> alkyl and Q is oxygen or sulphur, reacting a compound of formula (XIV):~~



~~wherein Hal is a suitable halogen, R<sup>2</sup>, R<sup>3</sup>, X<sup>1</sup>, X<sup>2</sup>, X<sup>3</sup>, X<sup>4</sup>, Z and R<sup>6</sup> are as defined in formula (I), with R<sup>1</sup>OH or R<sup>1</sup>SH in the presence of a suitable base;~~

and optionally after (a), (b), or (c), (d), (e), (f), (g), (h) ~~or~~ (i) forming a pharmaceutically acceptable salt or solvate of the compound of formula (I) obtained.

7. (Presently amended) A pharmaceutical composition comprising a compound of formula (I), or a pharmaceutically acceptable salt or solvate thereof, as ~~claimed in any one of claims claim 1 to 4~~ in association with a pharmaceutically acceptable adjuvant, diluent or carrier.

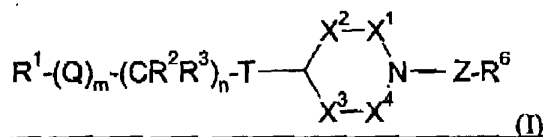
8. (Presently amended) A process for the preparation of a pharmaceutical composition as claimed in claim 7 which comprises mixing a compound of formula (I), or a pharmaceutically acceptable salt or solvate thereof, as ~~claimed in any one of claims claim 1 to 4~~ with a pharmaceutically acceptable adjuvant, diluent or carrier.

9-10. (Cancelled)

11. (Presently Amended) A method of treating ~~an inflammatory disease~~ asthma in a patient suffering from, or at risk of, said disease, which comprises administering to the patient a therapeutically effective amount of a compound of formula (I), or a pharmaceutically acceptable salt thereof, or solvate thereof, or a solvate of a salt thereof, ~~as defined claim 10.~~

Applicant : Stephen Thom et al.  
 Serial No. : 10/069,215  
 Filed : February 22, 2002  
 Page : 9 of 11

Attorney's Docket No.: 06275-244US1 / A 2214-1P US



wherein

Z is CR<sup>4</sup>R<sup>5</sup>, wherein R<sup>4</sup> and R<sup>5</sup> are CH<sub>2</sub>;

R<sup>1</sup> represents a 3- to 14-membered saturated or unsaturated ring system which comprises up to two ring carbon atoms that form carbonyl groups and which further comprises up to 4 ring heteroatoms independently selected from nitrogen, oxygen and sulphur, wherein the ring system is optionally substituted by one or more substituents independently selected from: halogen, cyano, nitro, oxo, hydroxyl, C<sub>1</sub>-C<sub>8</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> hydroxyalkyl, C<sub>1</sub>-C<sub>6</sub> haloalkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy(C<sub>1</sub>-C<sub>6</sub> alkyl), C<sub>3</sub>-C<sub>7</sub> cycloalkyl(C<sub>1</sub>-C<sub>6</sub> alkyl), C<sub>1</sub>-C<sub>6</sub> alkylthio(C<sub>1</sub>-C<sub>6</sub> alkyl), C<sub>1</sub>-C<sub>6</sub> alkylcarbonyloxy(C<sub>1</sub>-C<sub>6</sub> alkyl), C<sub>1</sub>-C<sub>6</sub> alkylS(O)<sub>2</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), aryl(C<sub>1</sub>-C<sub>6</sub> alkyl), heterocyclyl(C<sub>1</sub>-C<sub>6</sub> alkyl), arylS(O)<sub>2</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), heterocyclylS(O)<sub>2</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)S(O)<sub>2</sub>, heterocyclyl(C<sub>1</sub>-C<sub>6</sub> alkyl)S(O)<sub>2</sub>, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, carboxy-substituted C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>1</sub>-C<sub>6</sub> haloalkoxy, C<sub>1</sub>-C<sub>6</sub> hydroxyalkoxy, C<sub>1</sub>-C<sub>6</sub> alkylcarboxy-substituted C<sub>1</sub>-C<sub>6</sub> alkoxy, aryloxy, heterocycliloxy, C<sub>1</sub>-C<sub>6</sub> alkylthio, C<sub>3</sub>-C<sub>7</sub> cycloalkyl(C<sub>1</sub>-C<sub>6</sub> alkylthio), C<sub>3</sub>-C<sub>6</sub> alkynylthio, C<sub>1</sub>-C<sub>6</sub> alkylcarbonylamino, C<sub>1</sub>-C<sub>6</sub> haloalkylcarbonylamino, SO<sub>3</sub>H, -NR<sup>7</sup>R<sup>8</sup>, -C(O)NR<sup>23</sup>R<sup>24</sup>, S(O)<sub>2</sub>NR<sup>18</sup>R<sup>19</sup>, S(O)<sub>2</sub>R<sup>20</sup>, R<sup>25</sup>C(O), carboxyl, C<sub>1</sub>-C<sub>6</sub> alkoxy-carbonyl, aryl and heterocyclyl;

wherein the foregoing aryl and heterocyclyl moieties are optionally substituted by one or more of halogen, oxo, hydroxy, nitro, cyano, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> haloalkyl, phenyl(C<sub>1</sub>-C<sub>6</sub> alkyl), C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>1</sub>-C<sub>6</sub> haloalkoxy, S(O)<sub>2</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), C(O)NH<sub>2</sub>, carboxy or C<sub>1</sub>-C<sub>6</sub> alkoxy-carbonyl;

m is 0;

n is 2;

each R<sup>2</sup> and R<sup>3</sup> independently represents a hydrogen atom or a C<sub>1</sub>-C<sub>4</sub> alkyl group, or (CR<sup>2</sup>R<sup>3</sup>)<sub>n</sub> represents C<sub>3</sub>-C<sub>7</sub> cycloalkyl optionally substituted by C<sub>1</sub>-C<sub>4</sub> alkyl;

T represents a group C(O)NR<sup>10</sup>;

X<sup>1</sup>, X<sup>2</sup>, X<sup>3</sup> and X<sup>4</sup> are, independently, CH<sub>2</sub>;

R<sup>4</sup> and R<sup>5</sup> each independently represent a hydrogen atom or a C<sub>1</sub>-C<sub>4</sub> alkyl group;



Applicant : Stephen Thom et al.  
 Serial No. : 10/069,215  
 Filed : February 22, 2002  
 Page : 10 of 11

Attorney's Docket No.: 06275-244US1 / A 2214-1P US

R<sup>6</sup> is phenyl optionally substituted by one or more of: halogen, cyano, nitro, oxo, hydroxyl, C<sub>1</sub>-C<sub>8</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> hydroxyalkyl, C<sub>1</sub>-C<sub>6</sub> haloalkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy(C<sub>1</sub>-C<sub>6</sub> alkyl), C<sub>3</sub>-C<sub>7</sub> cycloalkyl(C<sub>1</sub>-C<sub>6</sub> alkyl), C<sub>1</sub>-C<sub>6</sub> alkylthio(C<sub>1</sub>-C<sub>6</sub> alkyl), C<sub>1</sub>-C<sub>6</sub> alkylcarbonyloxy(C<sub>1</sub>-C<sub>6</sub> alkyl), C<sub>1</sub>-C<sub>6</sub> alkylS(O)<sub>2</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), aryl(C<sub>1</sub>-C<sub>6</sub> alkyl), heterocyclyl(C<sub>1</sub>-C<sub>6</sub> alkyl), arylS(O)<sub>2</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), heterocyclylS(O)<sub>2</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)S(O)<sub>2</sub>, heterocyclyl(C<sub>1</sub>-C<sub>6</sub> alkyl)S(O)<sub>2</sub>, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, carboxy-substituted C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>1</sub>-C<sub>6</sub> haloalkoxy, C<sub>1</sub>-C<sub>6</sub> hydroxyalkoxy, C<sub>1</sub>-C<sub>6</sub> alkylcarboxy-substituted C<sub>1</sub>-C<sub>6</sub> alkoxy, aryloxy, heterocyclfloxy, C<sub>1</sub>-C<sub>6</sub> alkylthio, C<sub>3</sub>-C<sub>7</sub> cycloalkyl(C<sub>1</sub>-C<sub>6</sub> alkylthio), C<sub>3</sub>-C<sub>6</sub> alkynylthio, C<sub>1</sub>-C<sub>6</sub> alkylcarbonylamino, C<sub>1</sub>-C<sub>6</sub> haloalkylcarbonylamino, SO<sub>3</sub>H, -NR<sup>16</sup>R<sup>17</sup>, -C(O)NR<sup>21</sup>R<sup>22</sup>, S(O)<sub>2</sub>NR<sup>13</sup>R<sup>14</sup>, S(O)<sub>2</sub>R<sup>15</sup>, R<sup>26</sup>C(O), carboxyl, C<sub>1</sub>-C<sub>6</sub> alkoxy-carbonyl, aryl and heterocyclyl; wherein the foregoing aryl and heterocyclyl moieties are optionally substituted by one or more of halogen, nitro, cyano, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> haloalkyl, phenyl(C<sub>1</sub>-C<sub>6</sub> alkyl), C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>1</sub>-C<sub>6</sub> haloalkoxy, S(O)<sub>2</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), C(O)NH<sub>2</sub>, carboxy or C<sub>1</sub>-C<sub>6</sub> alkoxy-carbonyl;

R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup>, R<sup>10</sup>, R<sup>11</sup>, R<sup>13</sup>, R<sup>14</sup>, R<sup>16</sup>, R<sup>17</sup>, R<sup>18</sup>, R<sup>19</sup>, R<sup>21</sup>, R<sup>22</sup>, R<sup>23</sup> and R<sup>24</sup> are, independently hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> haloalkyl, C<sub>1</sub>-C<sub>6</sub> hydroxyalkyl, C<sub>3</sub>-C<sub>7</sub> cycloalkyl, C<sub>3</sub>-C<sub>7</sub> cycloalkyl(C<sub>1</sub>-C<sub>4</sub> alkyl) or phenyl(C<sub>1</sub>-C<sub>6</sub> alkyl); and,

R<sup>15</sup> and R<sup>20</sup> are, independently, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> hydroxyalkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, C<sub>3</sub>-C<sub>7</sub> cycloalkyl(C<sub>1</sub>-C<sub>4</sub> alkyl) or C<sub>1</sub>-C<sub>6</sub> alkyl optionally substituted by phenyl;

R<sup>25</sup> and R<sup>26</sup> are, independently, C<sub>1</sub>-C<sub>6</sub> alkyl or phenyl (optionally substituted by one or more of halogen, nitro, cyano, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> haloalkyl, phenyl(C<sub>1</sub>-C<sub>6</sub> alkyl), C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>1</sub>-C<sub>6</sub> haloalkoxy, S(O)<sub>2</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), C(O)NH<sub>2</sub>, carboxy or C<sub>1</sub>-C<sub>6</sub> alkoxy-carbonyl).